Association of Tuberculous Endometritis with Infertility and Other Gynecological Complaints of Women in India

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Endometrial biopsy samples derived from 393 patients with assorted gynecological complaints were investigated for mycobacterial infection. By employment of four different techniques, mycobacterial pathogens were detected irrespective of the nature/type of clinical complaint. Mycobacterium tuberculosis was the predominant pathogen detected among the samples investigated.

Tuberculosis occurs worldwide and causes widespread morbidity and mortality. Pulmonary and extrapulmonary sites are known to be associated with Mycobacterium tuberculosis infection. In fact, it is well known that pulmonary tuberculosis patients go on to develop extrapulmonary tuberculosis. One such manifestation is the occurrence of female genital tuberculosis (FGTB). The spread of the pathogen to fallopian tubes, endometria, and ovaries, leading to a variety of clinical conditions, has been described previously (1, 8, 15). The present study was undertaken to detect mycobacterial infection in endometrial biopsy (EB) samples collected from patients registered in the gynecological outpatient department of the All India Institute of Medical Sciences, New Delhi, India.

Three hundred ninety-three patients attending the obstetrics and gynecology outpatient department of the All India Institute of Medical Sciences were included in the study. Of these, 285 were infertility patients, 80 had menstrual dysfunction complaints, 17 had chronic lower abdominal or pelvic pain, and the remaining 11 were patients with complaints such as ovarian cyst, fibroid, prolapsed uterus, and postrecanalization. The EB samples were processed as described by Chakravorty et al. (3). Randomly selected EB samples showing dual bands (116 bp and 89 bp) were cloned into the pGEMT vector by using a TA cloning kit (Promega). The clones were sequenced at the DNA sequencing facility, South Campus Delhi University, New Delhi, India.

The detection and identification of M. tuberculosis and M. bovis in representative EB specimens are depicted in Fig. 1. N-PCR-amplified products equivalent to 116 bp were obtained for five of the seven samples (lanes 1 to 3, 7, and 8). These samples were considered to be infected with M. tuberculosis. A representative sample depicting mixed infection with M. tuberculosis and M. bovis is shown in Fig. 1, lane 14. Samples with dual bands were eluted and sequenced. The sequences of the dual bands corresponding to 116 and 89 bp matched those of the C-terminal parts of the hupB genes of M. tuberculosis and M. bovis, respectively, as described previously (14).

Among EB samples, differences between results for detection of AFB, histopathological evidence of tuberculosis infection, isolation by culture, and detection of M. tuberculosis and M. bovis by N-PCR were observed (Table 1). Of the 393 EB extracts collected, AFB were detected in 20 (20/393; 5.1%), including those from patients with chronic lower abdominal or pelvic pain (2/17; 11.8%), infertility (16/285; 5.6%), and men...
strual dysfunction complaints (2/80; 2.5%). Granulomatous tissue reactions compatible with tuberculosis were observed exclusively in seven EB samples derived from infertile patients (7/220; 3.2%). Mycobacteria were isolated from 11 samples by culture (11/262; 4.2%). Nine strains were lost on subculture. (7/220; 3.2%). Mycobacteria were isolated from 11 samples by culture (11/262; 4.2%). Nine strains were lost on subculture.

<table>
<thead>
<tr>
<th>Clinical category (no. of patients)</th>
<th>No. of positive samples/no. tested (%)</th>
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<tbody>
<tr>
<td>Infertility* (285)</td>
<td>16/285 (5.6)</td>
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<tr>
<td>Menstrual dysfunction* (80)</td>
<td>2/80 (2.5)</td>
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<tr>
<td>Chronic lower abdominal or pelvic pain (17)</td>
<td>2/17 (11.8)</td>
</tr>
<tr>
<td>Miscellaneous§ (11)</td>
<td>0</td>
</tr>
<tr>
<td>Total (393)</td>
<td>20/393 (5.1)</td>
</tr>
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* Detection of AFB was done by auramine O staining of biopsy extracts.
§ Hematoxylin-and-eosin-stained EB sections were examined for tissue reactions compatible with tuberculosis.
§ Growth on Lowenstein-Jensen with pyruvate on solid medium at 37°C.
§ EB samples were taken from patients unable to become pregnant after a minimum of 1 year of attempting through unprotected intercourse.
§ Menstrual dysfunctions such as polymenorrhagia; amenorrhea (primary or secondary); oligomenorrhea; menorrhagia; and irregular, postmenstrual, continuous, or dysfunctional uterine bleeding.
§ Chronic lower abdominal or pelvic pain.
§ Miscellaneous complaints, such as ovarian cyst, uterine fibroid, prolapsed uterus, endometiosis, and postrecanalization.

The results for the various clinical conditions and techniques used in the study for detection of mycobacteria in the samples revealed that mycobacteria were detected by all the methods used in infertility cases. In cases of patients with menstrual dysfunction, mycobacteria were detected by only three methods, namely, AFB microscopy, isolation by culture, and N-PCR. In these individuals, no evidence of granulomatous reactions compatible with ongoing mycobacterial infection was detected. With acknowledgment that isolation of mycobacteria

is the gold standard for diagnosis of tuberculosis, eight isolates were obtained from infertility cases, two from patients with menstrual disorders, and one from a patient with an ovarian cyst. Similarly, N-PCR results for patients in all categories were positive. The highest percentage of positivity was for infertility cases (111/285; 39%). These results show that infertility with mycobacterial infection is a significant clinical problem in India. The prevalence of FGTB in infertility clinics has been reported to range from 1 to 19% (2, 11, 13). In addition to M. tuberculosis infection, M. bovis infection has been reported to occur in FGTB (4, 7). The failure to isolate M. bovis in the present study may be due to use of inappropriate media (5, 6). Nonspecific clinical presentation, inefficacy of laboratory diagnostic tests, and inaccessibility of reproductive clinics have resulted in underreporting of FGTB. Hence, patients with complaints of infertility and other gynecological complaints must necessarily be investigated for tuberculosis of the genital tract. The N-PCR, histopathology, and culture results confirm that infertility is a common clinical condition associated with FGTB.

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REFERENCES